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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SEHARASEYON, JEGATHEESAN	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,524	EATON ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/10/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-6 are pending and under consideration. The claims are drawn to antibodies that bind to PRO1013 polypeptide of SEQ ID NO: 22.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). Applicant is required to provide a paper copy of the CRF in response to the Office Action.

Information Disclosure Statement

4. The information disclosure statement, filed 9/10/2002, has been considered. The BLAST results demonstrate that applicants are aware of polynucleotides with identity/homology to the one claimed herein. However, as the BLAST results do not give sufficient identifying information, the Examiner cannot determine if said sequences constitute prior art.

Priority Determination

5. The claimed protein has no utility, see rejection below. Accordingly, priority under 35 U.S.C 120 is set at the instant filing date, 5/2/02.

Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to the date recited above which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of, and fully enabled fo,r prior to that date.

Rejections under 35 U.S.C. §101 and §112:

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

The claims are directed to antibodies that bind the protein of SEQ ID NO: 22. The specification contains numerous asserted utilities for the claimed antibodies, including use to identify molecules that bind to PRO1013 (including agonists and antagonists), diagnostic assays, affinity purification, and for the therapeutic purposes. The utilities that pertain solely to polynucleotides (e.g. hybridization, chromosome and gene mapping, anti-sense) would not convey utility to the encoded protein or the antibody.

With respect to the remaining utilities, none of these asserted utilities is specific for the disclosed PRO1013 protein, as each of the aforementioned utilities could be asserted for any naturally occurring protein, and further, as none of the asserted utilities requires any feature or activity that is specific to the disclosed PRO1013.

The specification asserts that PRO1013 is an unspecified secreted transmembrane polypeptide. However, this family of proteins does not possess a common utility, but rather the proteins that can be broadly classified and have different activities, that confer different uses on them. Accordingly, the mere identification of a protein as belonging to a family, while indicative of evolutionary relatedness, is not indicative of function, nor by extension, of utility. The structure of the putative PRO1013 peptide is briefly discussed in Figure 22, as having a signal peptide, corresponding to about amino acids 1-19, potential N-glycosylation site, corresponding to about amino acids 75-79 and 322-326. In addition, the figure identifies a growth factor and cytokine receptor family domain, corresponding to about amino acids 134-150. However, there is no functional characteristic associated with these motifs, hence the mere observation that they exist is not probative of function or utility. Further, there is no disclosure that the protein is expected to be a transmembrane protein, nor of any extracellular domain. There is no biological activity, expression pattern, phenotype, disease or condition, ligand, binding partner, any other specific feature that is disclosed as being associated with PRO1013. Without any information as to the specific properties of PRO1013, the mere identification of such as having homology to a secreted transmembrane protein is not sufficient to impart any particular utility to the claimed antibodies.

The polynucleotide (cDNA) of the instant invention is disclosed to be highly expressed in normal stomach compared to the stomach tumor based on the PCR amplification of cDNA libraries (see page 141), however, the specification does not disclose that the polypeptide is over more highly expressed in normal stomach vs. stomach tumor tissue. Thus, the specification asserts that the polynucleotide encoding PRO1013 polypeptide being more highly expressed in normal stomach vs. stomach tumor renders the molecule useful for the diagnosis as well as a therapeutically as a target for the treatment (see page 140). There is no supporting evidence to indicate that the polypeptide encoded by the nucleotide of the instant invention is more highly expressed in the normal tissue compared to the tumor tissue and as such one of skill in the art would conclude that it is not supported by a substantial asserted utility or a well-established utility. Although, the specification claims polynucleotide is more highly expressed in normal vs. tumor tissue, it is not clear if this tumor is malignant (cancerous) or benign. In addition, the specification does not teach what is the normal level of expression; does not indicate how high the expression is (compared to what?); and does not provide a statistical correlation to the expression profile (for example, there is no indication of how many samples were compared to study the expression). Furthermore, if the tumor is malignant, the specification fails to describe the type or kind of stomach tumor (for example, is it an adenocarcinoma or renal cell carcinoma etc.). Without knowing the identity of the tumor, one of skill in art cannot use the protein or antibodies for diagnosis or therapeutic purposes as asserted. The specification does not disclose a correlation between any specific disorder and the altered level or form of the

claimed polypeptides. Also, the specification does not predict whether the polypeptides would have high or low expression in a specific, diseased tissue compared to the healthy tissue control. In addition, the specification does not teach or describe the function of this yet to identified polypeptide. With respect to the remaining utilities, none of these asserted utilities is specific for the disclosed PRO1013 encoding polypeptides, as each of the aforementioned utilities could be asserted for any naturally occurring polypeptides, and further, as none of the asserted utilities requires any feature or activity that is specific to the disclosed PRO1013 polypeptides.

Cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes (see Sen, 2000, Curr. Opin. Oncol. 12: 82-88). The data presented in the instant specification are not corrected for aneuploidy. Higher amplification of a gene does not necessarily mean higher expression or lower expression in a tissue, but can merely be an indication that the cancer tissue is aneuploid. The preliminary data of the instant invention was not supported by further analysis of mRNA or protein expression, for example. Also, the literature reports that it does not necessarily follow that an increase in gene copy number results in increased gene expression and increased polypeptide expression, such that the claimed polypeptides would be useful for diagnosis of cancer or as a drug target. This fact is documented by Pennica et al. (1998, PNAS USA 95:14717-14722). In addition, they also observed that there was no correlation between WISP-2 mRNA expression and colon tumors. Furthermore they disclose that:

> "An analysis of *WISP*-1 gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP*-3 RNA was seen in the absence of DNA amplification. In contrast, *WISP*-2 DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient."

See p. 14722, second paragraph of left column; pp. 14720-14721, "Amplification and Aberrant Expression of *WISPs* in Human Colon Tumors." For example, WISP-2 RNA expression was significantly lower in the tumor than the mucosa (see p. 14721). Therefore, cDNA expression data pertaining to PRO1013 polynucleotides do not necessarily indicate anything significant regarding the claimed PRO1013 polypeptides. Thus, the data does not support the implicit assertion that the nucleotide encoding PRO1013 can be used in cancer diagnosis or therapy. Significant further research would have been required of the skilled artisan to determine why PRO1013 is more highly expressed in normal tissue compared to tumor tissue to the extent that it could be used as a cancer diagnostic, and thus the implicitly asserted utility is not substantial.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed the polypeptides.

"Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." Brenner v. Manson, 148 USPQ: at 696.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7a. Claims 1-6 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9a. Claim 1 states that the claimed antibody "binds" the protein of SEQ ID NO: 22, whereas dependent claim 6 states that the antibody "specifically binds". The term "specifically" in claim 6 is a relative term that renders the claim indefinite. The term "specifically" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be

reasonably apprised of the scope of the invention. Further, the antibodies would presumably be of no use if they did not bind to the protein of SEQ ID NO: 22 with specificity; therefore, it must be presumed that there is some level of specificity implicit in all the claims. As the difference between "binds" and "specifically binds" cannot be determined, the metes and bounds of all the claims are unclear. Change of "specifically" would be remedial, but then claim 6 would be a duplicate of claim 1.

Claim Rejections - 35 USC § 102

Priority is set at the instant filing date, 5/2/2002, as no disclosure to which priority is claimed meets the requirements of 35 U.S.C 101 and 112, first paragraph.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

10a. Claims 1-6 are rejected under 35 U.S.C. 102(e) as being anticipated by Edwards et al. (U.S. Patent No: 6,639,063).

SEQ ID NO: 3917 described by Edwards et al has 100% identity over first 151 amino acids of SEQ ID NO: 22 of the instant invention (see Appendix A). In addition, Edwards et al. also describe monoclonal antibodies, humanized antibodies, antibody fragments and labelled antibodies (columns 71-95). Therefore, claims 1-6 directed to antibodies are anticipated by Edwardsl et al. (U.S. Patent No: 6,639,063).

11. No claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS

GARY KUNZ
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